**eTable 1.** Associations between orofacial cleft status and lower respiratory tract infections stratified by potential mediator variables

| | | | n | Incidence | Incidence proportion (%) |
|---|---|---|---|---|---|
| History of any surgery under general anesthesia | None | Control group | 63,563 | 4,123 | 6.5 |
| | | Infants with CLP | 6 | 2 | 33.3 |
| | | Infants with CL | 6 | 1 | 16.7 |
| | | Infants with CP | 29 | 2 | 6.9 |
| | At least once | Control group | 701 | 58 | 8.3 |
| | | Infants with CLP | 52 | 6 | 11.5 |
| | | Infants with CL | 36 | 5 | 13.9 |
| | | Infants with CP | 2 | 0 | 0.0 |
| Birthweight | Normal birthweight (2500–4000 g) | Control group | 69,867 | 4,465 | 6.4 |
| | | Infants with CLP | 49 | 6 | 12.2 |
| | | Infants with CL | 31 | 6 | 19.4 |
| | | Infants with CP | 32 | 1 | 3.1 |
| | Low birthweight (<2500 g) | Control group | 5,954 | 353 | 5.9 |
| | | Infants with CLP | 10 | 2 | 20.0 |
| | | Infants with CL | 10 | 1 | 10.0 |
| | | Infants with CP | 2 | 1 | 50.0 |
| | High birthweight (≥4000 g) | Control group | 654 | 42 | 6.4 |
| | | Infants with CLP | - | - | - |
| | | Infants with CL | 1 | 0 | 0.0 |
| | | Infants with CP | - | - | - |
| Accumulated breastfeeding duration | 0 month | Control group | 1,999 | 125 | 6.3 |
| | | Infants with CLP | 10 | 0 | 0.0 |
| | | Infants with CL | 2 | 1 | 50.0 |
| | | Infants with CP | 8 | 1 | 12.5 |
| | 1 to 6 months | Control group | 15,865 | 1,306 | 8.2 |

| | | | | |
|---|---|---|---|---|
| | Infants with CLP | 37 | 7 | 18.9 |
| | Infants with CL | 10 | 2 | 20.0 |
| | Infants with CP | 14 | 1 | 7.1 |
| 7 to 12 months | Control group | 58,656 | 3,432 | 5.9 |
| | Infants with CLP | 12 | 1 | 8.3 |
| | Infants with CL | 30 | 4 | 13.3 |
| | Infants with CP | 12 | 0 | 0.0 |

CL, cleft lip; CLP, cleft lip and palate; CP, cleft palate only.

**eTable 2.** Missing values for each variable

| Variables | Number of missing | | Types of variable in the imputation (Categorical or continuous variables) |
|---|---|---|---|
| | n | % | |
| Orofacial clefts | 0 | 0.0 | Categorical |
| Maternal age at delivery | 4 | 0.0 | Categorical |
| Marital status during pregnancy | 821 | 1.0 | Categorical |
| Maternal active smoking during pregnancy | 1,048 | 1.3 | Categorical |
| Frequencies of maternal passive smoking during pregnancy | 848 | 1.0 | Categorical |
| Maternal educational attainment | 975 | 1.2 | Categorical |
| Annual household income during pregnancy | 6,106 | 7.5 | Categorical |
| Sex of the infant | 0 | 0.0 | Categorical |
| Season of birth | 0 | 0.0 | Categorical |
| Infant passive smoking status at one month of age | 652 | 0.8 | Categorical |
| Receiving routine vaccines in the National Immunization Program at 1 year of age | 0 | 0.0 | Categorical |
| Receiving influenza virus vaccines at 1 year of age | 0 | 0.0 | Categorical |
| Number of children living together at 1 year of age | 0 | 0.0 | Categorical |
| Attending nursery school at 6 months of age | 348 | 0.4 | Categorical |
| History of any surgery under general anesthesia | 12,943 | 15.9 | Categorical |
| Birthweight | 48 | 0.1 | Categorical |
| Accumulated breastfeeding duration | 0 | 0.0 | Categorical |
| Lower respiratory tract infections until 12 months of age | 0 | 0.0 | Categorical |

The weighted average methods were used, and the number of neighbors was defined as 3.

**eTable 3.** Associations between orofacial cleft status and lower respiratory tract infections from available-case analysis

| | | | | Crude model (n=81,535) | | Adjusted Model[a] (n=73,365) | | Adjusted Model[a] + Accumulated breastfeeding duration (n=73,365) | | Percentage change by accumulated breastfeeding duration[b] |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | Incidence | Incidence proportion (%) | IRR | 95% CI | IRR | 95% CI | IRR | 95% CI | |
| Control group (reference) | 81,383 | 4,863 | 6.0 | 1.00 | - | 1.00 | - | 1.00 | - | |
| Infants with CLP | 67 | 8 | 11.9 | 2.00 | 1.04, 3.83 | 2.51 | 1.38, 4.58 | 2.29 | 1.26, 4.15 | 14.6 |
| Infants with CL | 49 | 7 | 14.3 | 2.39 | 1.20, 4.75 | 2.39 | 1.05, 5.41 | 2.42 | 1.07, 5.46 | -2.2 |
| Infants with CP | 36 | 2 | 5.6 | 0.93 | 0.24, 3.58 | 1.12 | 0.29, 4.28 | 1.06 | 0.28, 4.10 | 50.0 |

CI, confidence interval; CL, cleft lip; CLP, cleft lip and palate, CP, cleft palate only; IRR, incidence risk ratio.

[a]Adjusted Model included factors such as maternal age at delivery, marital status during pregnancy, maternal active smoking during pregnancy, frequencies of maternal passive smoking status during pregnancy, maternal educational attainment, annual household income during pregnancy, sex of the infant, season of birth, infant passive smoking status at one month of age, receiving routine vaccines in the National Immunization Program at 1 year of age, receiving influenza virus vaccines at 1 year of age, number of children living together at 1 year of age, and attending nursery school at 6 months of age.

[b]The percentage change by each potential mediator variable was calculated using the formula $(IRR_{\text{adjusted model}}-IRR_{\text{adjusted model with a potential mediator variable}})/(IRR_{\text{adjusted model}}-1)*100$.